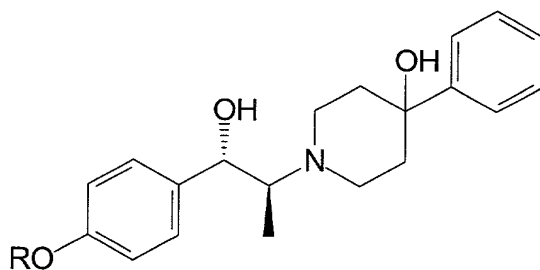
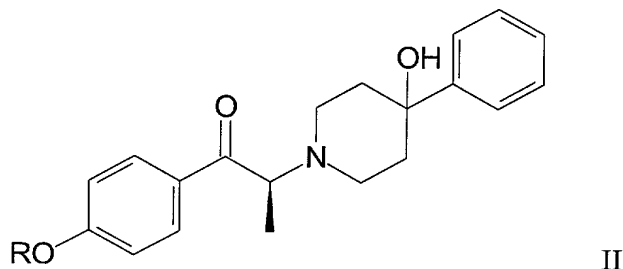


**CLAIMS:**

1. A process for the preparation of a nonracemic diastereomer selected from 1-(4-hydroxy-phenyl)-2-(4-hydroxy-4-phenyl-piperidin-1-yl)-1-propanol compounds of the structural formula I and stereoisomers thereof,



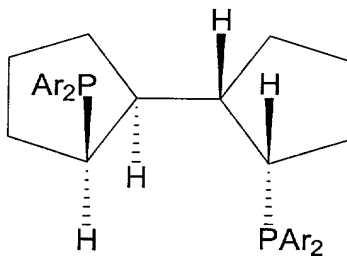
wherein R is selected from hydrogen and hydroxyl protecting groups, comprising hydrogenating a corresponding nonracemic ketone selected from 1-(4-hydroxy-phenyl)-2-(4-hydroxy-4-phenyl-piperidin-1-yl)-1-propanone compounds of the structural formula II and enantiomers thereof,



in the presence of a catalyst system comprising ruthenium, a nonracemic diphosphine ligand, a bidentate amine ligand selected from amino-thioethers and achiral diamines, and a base.

2. The process of claim 1 wherein the nonracemic diphosphine ligand comprises a 2,2'-bis(diorganophosphino)-1,1'-bis(cyclic) structure.

3. The process of claim 2 wherein the nonracemic diphosphine ligand is selected from enantiomers of diphosphine ligands having the structural formula



wherein Ar is an aryl group.

2014-09-23 09:28:50

- 1                    4.        The process of claim 3 wherein Ar is phenyl.
- 1                    5.        The process of claim 1 wherein the bidentate amine ligand is an amino-  
2 thioether.
- 1                    6.        The process of claim 5 wherein the amino-thioether is a  
2 2-(alkylthio)aniline.
- 1                    7.        The process of claim 6 wherein the 2-(alkylthio)aniline is selected  
2 from 2-(methylthio)aniline and 2-(ethylthio)aniline.
- 1                    8.        The process of claim 1 wherein the bidentate amine ligand is an achiral  
2 diamine.
- 1                    9.        The process of claim 8 wherein the achiral diamine comprises no chiral  
2 carbon centers.
- 1                    10.       The process of claim 8 wherein the achiral diamine is a 1,2-phenylene-  
2 diamine.
- 1                    11.       The process of claim 1 wherein the base is selected from basic  
2 inorganic and organic salts, alkylguanidines, aminophosphazenes, and proazaphosphatranes.
- 1                    12.       The process of claim 11 wherein the base is selected from  
2 alkylguanidines, aminophosphazenes, and proazaphosphatranes.
- 1                    13.       The process of claim 12 wherein the base is an alkylguanidine.
- 1                    14.       The process of claim 13 wherein the base is a pentaalkylguanidine.
- 1                    15.       The process of claim 1 wherein the hydroxyl protecting group is  
2 benzyl.
- 1                    16.       The process of claim 15 wherein the diastereomer is a *syn*-  
2 diastereomer.
- 1                    17.       The process of claim 16 wherein the *syn*-diastereomer is the (1*S*,2*S*)  
2 diastereomer.

1                   18.     The process of claim 16 wherein the *syn*-diastereomer is formed in at  
2     least about 90% diastereomeric excess.

1                   19.     A process for the preparation of (1*S*,2*S*)-1-(4-benzyloxy-phenyl)-2-(4-  
2     hydroxy-4-phenyl-piperidin-1-yl)-1- by catalytic hydrogenation of (2*S*)-1-(4-benzyl-phenyl)-  
3     2-(4-hydroxy-4-phenyl-piperidin-1-yl)-1-propanone using a catalyst system comprising  
4     ruthenium, a (*S,S,S,S*)-2,2'-bis-(diarylphosphino)-1,1'-dicyclopentane ligand, a 1,2-phenylene  
5     diamine ligand, and a base.

1                   20.     A process for the preparation of (1*S*,2*S*)-1-(4-benzyloxy-phenyl)-2-(4-  
2     hydroxy-4-phenyl-piperidin-1-yl)-1- by catalytic hydrogenation of (2*S*)-1-(4-benzyl-phenyl)-  
3     2-(4-hydroxy-4-phenyl-piperidin-1-yl)-1-propanone using a catalyst system comprising  
4     ruthenium, a (*S,S,S,S*)-2,2'-bis-(diarylphosphino)-1,1'-dicyclopentane ligand, a  
5     2-(alkylthio)aniline ligand, and a base.

201210 92825007  
10057826 012402